

## Hydrogen-Bond-Assisted Stereocontrol in Radical Polymerization of *N*-Isopropylacrylamide by Using Primary Alkyl Phosphate – Effect of Chain Length of Straight Ester Group

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Running Head: Stereocontrol in NIPAAm polymerization

**ABSTRACT:** Radical polymerizations of *N*-isopropylacrylamide (NIPAAm) were carried out in toluene at low temperatures in the presence of phosphoric acid esters such as trimethyl, triethyl (TEP), tri-*n*-propyl, and tri-*n*-butyl phosphates (TBP). Syndiotactic-rich poly(NIPAAm)s were obtained at the temperature range from  $-60^{\circ}\text{C}$  to  $0^{\circ}\text{C}$ , and particularly TEP provided the highest syndiotacticity (*racemo* diad = 65%) at  $-40^{\circ}\text{C}$ . On the other hand, lowering temperature reversed the stereoselectivity of the propagation reaction so that isotactic-rich poly(NIPAAm)s were obtained at  $-80^{\circ}\text{C}$ . In particular, TBP exhibited the most isotactic-specificity (*meso* diad = 57%). Job's plots for NIPAAm-TBP mixtures revealed that NIPAAm and TBP formed 1:1 complex at  $0^{\circ}\text{C}$  and predominantly 1:2 complex at  $-80^{\circ}\text{C}$  through a hydrogen-bonding interaction. Therefore, it is considered that the stereospecificity of NIPAAm polymerization should depend on the stoichiometry of the hydrogen-bond-assisted complex. Thus, the

mechanism for the present polymerization system was discussed.

**Keywords:** *N*-isopropylacrylamide; stereospecific polymerization; radical polymerization; hydrogen bond; phosphate; tacticity;

## INTRODUCTION

Stereospecific polymerization has been received much attention so far, because stereoregularity of polymers significantly affects properties of polymers. In particular, methacrylates are intensively investigated in regard of stereospecificity of metal-mediated anionic or coordination polymerization and a wide range of stereoregular polymers has been synthesized.<sup>1-7</sup> However, there are few reports on stereospecific polymerization of acrylates,<sup>8,9</sup> although methyl group at  $\alpha$ -position of methacrylates is just replaced by hydrogen atom. Therefore, it has been accepted that the  $\alpha$ -methyl group is essential for the stereocontrol in polymerization of  $\alpha,\beta$ -unsaturated ester monomers.

On the contrary, several stereospecific anionic polymerizations of *N,N*-disubstituted acrylamides have been reported notwithstanding the lack of  $\alpha$ -methyl group,<sup>10-13</sup> whereas *N,N*-disubstituted methacrylamide, except for methacryloylaziridine,<sup>14</sup> cannot be polymerized by any methods. Furthermore, there are a few reports on stereocontrol based on the chirality<sup>15</sup> or the bulkiness<sup>16</sup> of the substituents even for radical polymerization of *N,N*-disubstituted acrylamide. On the other hand, radical polymerization of *N*-monosubstituted acrylamides gives atactic polymers regardless of the kinds of both the substituents and solvents, except for isotactic-specific polymerization in the presence of Lewis acids such as yttrium trifluoromethanesulfonate.<sup>17</sup> Thus, stereoregular polymers were prepared by an anionic polymerization of *N*-monosubstituted acrylamide, of which the acidic proton was protected.<sup>18,19</sup> Therefore, it has been suggested that the steric interaction by the second substituent at the amide nitrogen atom is another important factor for the stereocontrol

in polymerization of  $\alpha,\beta$ -unsaturated amide monomers.

Recently, we reported that radical polymerization of *N*-isopropylacrylamide (NIPAAm) in toluene at 0 °C gives a syndiotactic-rich poly(NIPAAm) in the presence of phosphoric acid derivatives such as trimethyl phosphate (TMP) and hexamethylphosphoramide (HMPA).<sup>20</sup> The *racemo* (*r*) diad increased up to 63% in the presence of a twofold amount of HMPA. This is the first example of a facile synthesis of syndiotactic-rich poly(NIPAAm) *via* a radical polymerization under the metal-free conditions. The NMR analysis of NIPAAm-HMPA mixtures demonstrated that NIPAAm and HMPA formed 1:1 complex through a hydrogen-bonding interaction. Thus, it is assumed that the coordinating HMPA behaved like the second substituent at the nitrogen amide atom and hence a syndiotactic-rich poly(NIPAAm) was obtained. In this article, radical polymerization of NIPAAm was carried out in the presence of primary alkyl phosphates, such as TMP, triethyl phosphate (TEP), tri-*n*-propyl phosphate (TPP), and tri-*n*-butyl phosphate (TBP), to investigate in detail the effect of bulkiness of the added Lewis base. Consequently, it was found that, besides syndiotactic-rich poly(NIPAAm), isotactic-rich poly(NIPAAm) were also obtained only by changing the polymerization temperature.

## EXPERIMENTAL

### Materials

NIPAAm was recrystallized from hexane-benzene mixture. Toluene was purified through washing with sulfuric acid, water, and 5% aqueous NaOH; this was followed by fractional distillation. Tri-*n*-butylborane (*n*-Bu<sub>3</sub>B) as a tetrahydrofuran (THF) solution (1.0M), TMP, TEP, TPP, and TBP were commercially obtained and used without further purification for polymerization reaction.

### Polymerizations

Typical polymerization procedure is as follows; NIPAAm (0.314 g, 2.8 mmol) was dissolved in toluene to prepare the 5 mL solution of 0.56 mol/L. Four milliliter of the solution was transferred to the glass ampoule and cooled at 0°C. The polymerization was initiated by adding *n*-Bu<sub>3</sub>B solution (0.22 ml) into the monomer solution. After 24h, the reaction was terminated with a small amount of THF solution of 2,6-di-*t*-butyl-4-methylphenol at polymerization temperature. The polymerization mixture was poured into a large amount of hexane or hexane-ethyl acetate mixture (9:1 vol:vol), and the precipitated polymer was collected by filtration, and dried *in vacuo*. The polymer yield was determined from the weight ratio of the obtained polymer and the feed monomer.

## Measurements

The <sup>1</sup>H and <sup>13</sup>C NMR spectra of NIPAAm monomer and/or TBP were measured in toluene-*d*<sub>8</sub> at -80°C to 60°C on an EX-400 spectrometer (JEOL Ltd.) operated at 400MHz for <sup>1</sup>H and at 100MHz for <sup>13</sup>C. The tacticities of the poly(NIPAAm)s were determined from <sup>1</sup>H NMR signals due to methylene group in chain measured in deuterated dimethyl sulfoxide (DMSO-*d*<sub>6</sub>) at 150°C. The molecular weights and molecular weight distributions of the polymers were determined by size exclusion chromatography (SEC) (HLC 8220 instrument (Tosoh Co.)) equipped with TSK gels (SuperHM-M and SuperHM-H (Tosoh Co.)) using dimethylformamide (LiBr 10 mmol/L) as an eluent at 40°C ([polymer] = 1.0 mg/mL, flow rate = 0.35 mL/min). The SEC chromatogram was calibrated with standard polystyrene samples.

## RESULTS AND DISCUSSION

### Radical Polymerization of NIPAAm in the Presence of Phosphates

Table 1 summarizes the results of radical polymerization of NIPAAm in toluene at low temperatures for 24h in the absence or presence of an equimolar amount of phosphate

such as TMP, TEP, TPP, and TBP. In the absence of phosphates, polymer yield drastically decreased as the polymerization temperature was lowered, probably because monomer and/or polymer were precipitated during the polymerization reaction. However, polymer yields increased even at low temperatures in the presence of phosphates, since the addition of an equimolar amount of phosphate improved the solubility of NIPAAm and/or poly(NIPAAm) in toluene. Furthermore, the addition of phosphate showed a tendency to decrease number-average molecular weights and molecular weight distributions of the obtained poly(NIPAAm)s.

<Table 1>

Figure 1 displays the relationship between polymerization temperature and *r* diad content of poly(NIPAAm) prepared in the absence or presence of an equimolar amount of phosphate. Atactic poly(NIPAAm)s were obtained regardless of the polymerization temperature in the absence of phosphates. However, the syndiotacticity was slightly increased by adding each phosphate and the maximums in the syndiotacticity were observed at  $-40^{\circ}\text{C}$  to  $-20^{\circ}\text{C}$  in the presence of phosphates except for TMP ( $-60^{\circ}\text{C}$ ). Both TMP and TEP influenced significantly the syndiotactic-specificity of NIPAAm polymerization, but TPP and TBP with longer chains exhibited less stereocontrol under the conditions. This result suggests that the straight-chain length of ester groups affects the stereoselectivity of the propagating reaction.

<Figure 1>

Then, NIPAAm polymerization was carried out in the presence of a twofold amount of each phosphate (Table 2). The addition of a twofold amount of phosphate improved the homogeneity of polymerization system so that poly(NIPAAm)s were

obtained quantitatively even at low temperatures except for the addition of TEP at  $-80^{\circ}\text{C}$  to  $-60^{\circ}\text{C}$ . Moreover, the increasing amount of an added phosphate resulted in the obvious tendency of the decrease in number-average molecular weight.

<Table 2>

Figure 2 portrays the relationship between polymerization temperature and  $r$  diad content of poly(NIPAAm) prepared in the absence or presence of a twofold amount of phosphate. As with an equimolar amount of phosphate, the addition of a twofold amount of phosphate increased the syndiotactic-specificity. Furthermore, the syndiotacticity increased with increasing the amount of an added phosphate, whereas the maximums in the syndiotacticity were observed at almost the same temperature range ( $-40^{\circ}\text{C} \sim -20^{\circ}\text{C}$ ). The dependence of the straight chain length on the stereoselectivity of the propagating reaction was more clearly observed, that is, TEP exhibited the better syndiotactic-specificity than TMP and the syndiotactic-specificity was reduced as the alkyl chain length became further longer.

<Figure 2>

Surprisingly, the isotacticity significantly increased by lowering the polymerization temperature to  $-80^{\circ}\text{C}$  in the presence of a twofold amount of phosphate. TEP exhibited the worse isotactic-specificity than TMP and the isotactic-specificity was enhanced as the straight chain was lengthened. This is the opposite tendency to that in syndiotactic-specificity at higher temperatures.

Thus, the amount of an added phosphate was further increased. Table 3 summarizes the polymerization results in the presence of a fourfold amount of phosphate. The polymer yield was kept high, although the increase in the amount of an added

phosphate not only decreased the number-average molecular weights of poly(NIPAAm) but also encumbered the precipitation of poly(NIPAAm).

<Table 3>

Figure 3 demonstrates the relationship between polymerization temperature and *r* diad content of poly(NIPAAm) prepared in the absence or presence of a fourfold amount of phosphate. The tacticity dependence on the ester chain length was also observed. The increase in the syndiotacticity was further enhanced at  $-60^{\circ}\text{C}$  to  $0^{\circ}\text{C}$ . In particular, syndiotactic-rich poly(NIPAAm) with *r* diad = 65 % was obtained at  $-40^{\circ}\text{C}$  in the presence of TEP. This value is higher than that of poly(NIPAAm) obtained at  $0^{\circ}\text{C}$  in the presence of a twofold amount of HMPA.<sup>20</sup> Furthermore, the isotacticity was also enhanced at  $-80^{\circ}\text{C}$  and isotactic-rich poly(NIPAAm) with *meso* (*m*) diad 57 % was obtained in the presence of TBP. Figure 4 displays expanded  $^1\text{H}$  NMR spectra due to methylene and methine groups in main chain of poly(NIPAAm)s, of which stereoregularities are atactic, syndiotactic-rich, and isotactic-rich, respectively. Sufficient changes were observed in signals due to both  $-\text{CH}_2-$  and  $-\text{CH}-$  groups.

<Figure 3>

<Figure 4>

### **Equilibrium Constant of the Complex between NIPAAm and Phosphates**

As previously reported,<sup>20</sup> NIPAAm and HMPA formed 1:1 complex through a hydrogen-bonding interaction. Therefore, we determined the equilibrium constant of the NIPAAm-phosphate complex, on the assumption that NIPAAm and phosphates also form 1:1 complex. The equilibrium constant (*K*) of the NIPAAm-phosphate complex was determined by changes in the  $^1\text{H}$  NMR chemical shift of amide proton of NIPAAm.

Figure 5 demonstrates the relationship between the change in the chemical shift and the ratio of [phosphate]<sub>0</sub>/[NIPAAm]<sub>0</sub> with the constant concentration of [NIPAAm]<sub>0</sub> (5.0 × 10<sup>-2</sup> mol/L) in toluene-*d*<sub>8</sub> at several temperatures. The equilibrium constants (*K*) (Table 4) were determined by the analysis of the data in Figure 5 by a nonlinear least-squares fitting to the following eq. (1):<sup>21</sup>

$$\Delta\delta = \frac{\Delta\delta'}{2} (b - \sqrt{b^2 - 4X}) \quad (1)$$

$$b = 1 + X + \frac{1}{(K [NIPAAm]_0)}$$

$$X = [\text{phosphate}]_0 / [NIPAAm]_0$$

where  $\Delta\delta$  and  $\Delta\delta'$  are the changes in the chemical shift of amide proton of NIPAAm for the given solution and a saturated solution, respectively.

<Figure 5>

The equilibrium constants of phosphates were smaller than that of HMPA. For instance, the *K* for TEP, which exhibited the highest constant among the used phosphates, was 15.3 L/mol at 0°C, whereas the *K* for HMPA was 44.0 L/mol at 0°C.<sup>20</sup> Furthermore, the equilibrium constant for TEP was larger than that for TMP at each temperature and the constant *K* decreased gradually as the straight chain was lengthened. Thus, it is indicated that *K* also showed a dependence on chain length of ester groups, corresponding to the tendency observed in the tacticity change for NIPAAm polymerization in the presence of excess amounts of phosphates (cf. Figures 2 and 3).

<Table 4>

The *K* values below 0°C were not obtained, because the changes in the chemical shift of amide proton of NIPAAm were too small to evaluate the constants. Thus, we performed



van't Hoff's plots for the obtained  $K$  values as shown in Figure 6. The enthalpy ( $\Delta H$ ) and the entropy ( $\Delta S$ ) for the complex formation were determined (Table 5) from the following eq. (2):

$$\ln K = \frac{\Delta S}{R} - \frac{\Delta H}{RT} \quad (2)$$

where  $R$  is a gas constant (8.315 J/mol•K) and  $T$  is the absolute temperature (K). Thus, we calculated  $K$  values below 0°C, assuming that  $\Delta H$  is constant from -60°C to 60°C, and summarized the calculated values in Table 4 with the obtained values for 0°C to 60°C.

<Figure 6>

<Table 5>

Thus, by applying the  $K$  values to the polymerization conditions, we evaluated the degree of association ( $\alpha$ ) of NIPAAm as shown in Figure 7. In all the cases, the fraction of the complexed NIPAAm increased as the polymerization temperature was lowered. When an equimolar amount of each phosphate was added, the degree of association of NIPAAm was low and only 70% of NIPAAm formed the complex at 0°C even with TEP that exhibited the best association ability among the used phosphates. However, the addition of a twofold amount of each phosphate improved the complex formation and 78% of NIPAAm formed complex at 0°C even with TMP that exhibited the worst association ability among the used phosphates. Furthermore, NIPAAm only less than 10% was free at 0°C by adding a fourfold amount of each phosphate and the  $\alpha$  values were close to unity by lowering temperature.

<Figure 7>

### Stoichiometry of NIPAAm-Phosphate Complex

As mentioned above, TEP exhibited not only the highest syndiotactic-specificity but also the highest association ability among the used phosphates. This result suggests that the syndiotactic-specificity of NIPAAm polymerization depends on the ability of complex formation of phosphate. However, the maximums in the syndiotacticity were observed between  $-40^{\circ}\text{C}$  and  $-20^{\circ}\text{C}$ , although the  $\alpha$  values increased with decreasing the polymerization temperature. Moreover, isotactic-rich poly(NIPAAm)s were obtained at  $-80^{\circ}\text{C}$ . Thus, it is assumed that phosphates play a more complicated role in stereocontrol of NIPAAm polymerization.

<Figure 8>

To reinvestigate the stoichiometry of the NIPAAm-phosphate complex in more detail, we conducted  $^{13}\text{C}$  NMR analysis under the following conditions;  $[\text{NIPAAm}]_0 + [\text{TBP}]_0 = 0.25 \text{ mol/L}$ , in toluene- $d_8$  at desired temperatures. Figure 8 shows changes in the chemical shift of methylene carbon of NIPAAm when the fraction of  $[\text{NIPAAm}]_0$  was varied at  $0^{\circ}\text{C}$ . Thus, the stoichiometry of the complex was evaluated by Job's method (Figure 9) with the following eq. (3);<sup>22</sup>

$$[\text{NIPAAm} - \text{TBP}] = \frac{\delta(\text{CH}_2=) - \delta(\text{CH}_2=)_f}{\delta(\text{CH}_2=)_c - \delta(\text{CH}_2=)_f} \times [\text{NIPAAm}]_0 \quad (3)$$

where  $\delta(\text{CH}_2=)$  and  $\delta(\text{CH}_2=)_f$  are the chemical shifts of methylene carbon of the sample mixture and NIPAAm alone, respectively. As previously reported,<sup>20</sup> the chemical shift of NIPAAm alone also varied with the concentration (Figure 8), because NIPAAm itself also associates each other through a hydrogen-bonding interaction. Thus, the chemical shifts of NIPAAm alone at the corresponding concentration were applied as  $\delta(\text{CH}_2=)_f$ . The chemical shift for the saturated mixture ( $\delta(\text{CH}_2=)_c$ ) was calculated from the intercept of a linear dependence in Figure 8, since the saturation should be independent of

NIPAAm concentration. The maximum was observed at 0.5 of the  $[\text{NIPAAm}]_0$  fraction (Figure 9), although the precision was not high due to the small change in the chemical shift. Thus, it is considered that TBP forms 1:1 complex with NIPAAm at  $0^\circ\text{C}$  as well as HMPA.

<Figure 9>

At  $-80^\circ\text{C}$ , the change in the chemical shift of carbonyl carbon was large enough to be applied to Job's plots, whereas that of methylene carbon was too small. Thus, we applied the chemical shift of carbonyl carbon to Job's plots to evaluate the stoichiometry at  $-80^\circ\text{C}$ . Figure 10 demonstrates changes in the chemical shift of carbonyl carbon of NIPAAm in the presence of TBP ( $[\text{NIPAAm}]_0 + [\text{TBP}]_0 = 0.25 \text{ mol/L}$ ) and of NIPAAm alone at the corresponding concentration. The chemical shift was significantly shifted to up-field with the decrease in  $[\text{NIPAAm}]_0$  in the presence of TBP compared with in the absence of TBP. The plots roughly obeyed not a linear equation but a quadratic equation. Thus, the chemical shift for the saturated mixture ( $\delta(\text{C}=\text{O})_e$ ) was calculated from the intercept of a quadratic dependence in Figure 10. Unlike at  $0^\circ\text{C}$ , the maximum was observed between 0.33 and 0.4 of the  $[\text{NIPAAm}]_0$  fraction (Figure 11). This means that NIPAAm and TBP predominantly form 1:2 complex instead of 1:1 complex at  $-80^\circ\text{C}$ .

<Figure 10>

<Figure 11>

### **Proposed Mechanism of Stereospecific Radical Polymerization of NIPAAm in the Presence of Phosphates**

In general, methacrylic acid derivatives, such as methacrylates and *N*-monosubstituted

methacrylamides, give syndiotactic-rich polymers regardless of both polymerization temperature and the kind of solvents. On the other hand, acrylic acid derivatives, such as acrylates and *N*-monosubstituted acrylamides, give atactic polymers, even though polymerization conditions including temperature and solvent are extensively changed. Therefore, it has been accepted that the steric interaction by less bulky substituent at  $\alpha$ -position is one of the important factors in stereocontrol of vinyl polymerization.

In the previous paper,<sup>20</sup> we proposed the mechanism of syndiotactic-specific radical polymerization of NIPAAm in the presence of HMPA as follows; (1) NIPAAm forms 1:1 complex with the added HMPA and the extended methyl groups of HMPA generate a certain steric hindrance around  $\alpha$ -hydrogen atom; (2) the steric hindrance generated by HMPA is maintained even at the propagating radical, since the complexed NIPAAm transform to the corresponding propagating radical (Scheme 1); (3) the propagating reaction proceeds between the propagating radical and the monomer, both of which are coordinated by HMPA; (4) HMPA makes the less bulky side of  $\alpha$ -hydrogen atom apparently bulkier than that of amide group; (5) consequently syndiotactic-rich poly(NIPAAm) is prepared probably because the apparently less bulky amide group exhibits a significant steric interaction like  $\alpha$ -methyl group of methacrylic acid derivatives. The formation of syndiotactic-rich poly(NIPAAm) at higher temperature in the present system is also explainable with this mechanism. However, the proposed mechanism cannot explain the formation of isotactic-rich poly(NIPAAm) at  $-80^{\circ}\text{C}$ .

<Scheme 1>

It is well known that the syndiotactic-specificity decreases with an increase in the bulkiness of ester group of methacrylates, and extremely bulky derivatives such as triphenylmethyl methacrylate affords isotactic polymers even by a radical mechanism.<sup>23,24</sup> However, triphenylmethyl acrylate gives atactic polymers in spite of

the extremely bulky side chain,<sup>25</sup> although methyl group at  $\alpha$ -position of methacrylate is just replaced by hydrogen atom. Thus, it is assumed that the bulkiness of the bulkier substituent is also an important factor in stereocontrol of methacrylate polymerizations. We obtained new findings that 1:2 complex was predominantly formed at  $-80^{\circ}\text{C}$  in the present system (cf. Figure 11) and isotactic-rich poly(NIPAAm) was obtained at  $-80^{\circ}\text{C}$  (cf. Figure 3). Thus, we improve the above-mentioned mechanism as below.

In NIPAAm polymerization in the absence of Lewis base, the incoming monomer would approach to the propagating radical center as shown in Scheme 2 to reduce the steric repulsion between the amide group of monomer and the amide group at the chain end. However, the single bond near the chain end could rotate freely to reduce the steric repulsion between the bulkier substituents, amide groups, at the penultimate and chain-end monomeric units of the newly formed radical, since the  $\alpha$ -hydrogen atom at the chain end would be not bulky enough to fix the conformation near the propagating chain-end. In this case, the next incoming monomer can approach *via* two possible pathways, **a** and **b**, and a new incoming monomer *via* the **a** pathway should form *r* diad and that *via* the **b** pathway *m* diad. Thus, it is assumed that the easy rotation of the single bond near the chain end ascribes to non-stereospecificity of polymerization of acrylic acid derivatives.

<Scheme 2>

When phosphates were added, 1:1 complex formed predominantly at high temperatures. The phosphate coordinating to NIPAAm monomer makes the less bulky side of  $\alpha$ -hydrogen atom apparently bulkier than that of amide group as well as HMPA, although the influence of phosphate on syndiotacticity was smaller than that of HMPA probably because of the lower equilibrium constant. Therefore, the incoming monomer would approach to the propagating radical center as shown in Scheme 3 to reduce the

steric repulsion between the Lewis base coordinating to the monomer and the Lewis base at the chain end. Furthermore, the apparently less bulky substituent, amide group, would be significantly bulky enough to fix the conformation of the single bond near the chain end, based on the steric repulsion between the amide group at the chain end and the Lewis base at the penultimate monomeric unit. In this case, the steric hindrance of the Lewis base coordinating to the penultimate monomeric unit would also limit the approach *via* the **b** pathway by the next incoming monomer. Therefore, the next incoming monomer predominantly approaches *via* the **a** pathway, resulting in formation of syndiotactic-rich poly(NIPAAm).

<Scheme 3>

At lower temperatures, the fraction of 1:2 complex increased. As with 1:1 complex, the incoming monomer would approach to the propagating radical center as shown in Scheme 4 to reduce the steric repulsion between the Lewis bases coordinating to the monomer and the Lewis bases at the chain end. The second phosphate coordinating to NIPAAm-phosphate complex would increase the apparent bulkiness of the side of  $\alpha$ -hydrogen atom in addition. This steric change corresponds to the steric change in bulkiness of ester group of methacrylates. Consequently, the steric repulsion between the Lewis bases coordinating to the penultimate monomeric unit and the Lewis bases at the chain-end monomeric unit would be much larger than that between the Lewis bases coordinating to the penultimate monomeric unit and the less bulky substituent at the chain end. Thus, the newly formed propagating radical could transform again conformationally to reduce the steric repulsion between the Lewis bases coordinating to the penultimate and chain-end monomeric units as shown in Scheme 4. In this case, the steric hindrance of the Lewis bases coordinating to the penultimate monomeric unit prevents the radical from the propagation *via* the **a** pathway. Therefore, the next

incoming monomer predominantly approaches *via* the **b** pathway, resulting in formation of isotactic-rich poly(NIPAAm). If a propagating radical repeats such a propagating reaction *via* the **b** pathway with a conformational change, a polymer chain should grow up helically. This concept corresponds to the helical propagation in isotactic-specific radical polymerization of triphenylmethyl methacrylate.<sup>23</sup>

<Scheme 4>

## CONCLUSIONS

Radical polymerizations of NIPAAm were examined in the presence of several phosphates. It was found that the addition of phosphate increased the syndiotactic-specificity of NIPAAm polymerization as well as HMPA, although the effect of phosphate was smaller than that of HMPA. Furthermore, by lowering temperature, isotactic-rich poly(NIPAAm)s were obtained. The NMR analysis revealed that NIPAAm and phosphate form 1:1 complex at 0°C, but the fraction of 1:2 complex increased with a decrease in polymerization temperature. Thus, it was assumed that the stereospecificity of NIPAAm polymerization depended on the apparent bulkiness of the side of  $\alpha$ -hydrogen atom generated by the coordination of phosphate through a hydrogen-bonding interaction. The present polymerization system is the first example of stereocontrol from syndiotactic-rich to isotactic-rich in radical polymerization of NIPAAm only by changing the polymerization temperature. Further work is now under way to extend the present results to higher level of stereoregulation.

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## REFERENCES

1. Hatada, K.; Kitayama, T.; Ute, K. *Prog Polym Sci* 1988, 13, 189-276.
2. Kitayama, T.; Zhang, Y.; Hatada, K. *Polym J* 1994, 26, 868-872.
3. Hirano, T.; Yamaguchi, H.; Kitayama, T.; Hatada, K. *Polym J* 1998, 30, 767-769.
4. Farnham, W. B.; Hertler, W. U.S. Patent 4,728,706, 1988.
5. Yasuda, H.; Yamamoto, H.; Yokota, K.; Miyake, S.; Nakamura, A. *J Am Chem Soc* 1992, 114, 4908-4909.
6. Collins, S.; Ward, S. G. *J Am Chem Soc* 1992, 114, 5460-5462.
7. Chen, E. Y.-X. *J Polym Sci: Part A: Polym Chem* 2004, 42, 3395-3403.
8. Liu, W.; Nakano, T.; Okamoto, Y. *Polym J* 1999, 31, 479-481.
9. Tabuchi, M.; Kawauchi, T.; Kitayama, T.; Hatada, K. *Polymer* 2002, 43, 7185-7190.
10. Butler, K.; Thomas, P. R.; Tyler, G. J. *J Polym Sci* 1960, 48, 357-366.
11. Gia, H.; McGrath, J. E. *Polym Bull* 1980, 2, 837-840.
12. Xie, X.; Hogen-Esch, T. E. *Macromolecules* 1996, 29, 1746-1752.
13. Kobayashi, M.; Okuyama, S.; Ishizone, T.; Nakahama, S. *Macromolecules* 1999, 32, 6466-6477.
14. Okamoto, Y.; Yuki, H. *J Polym Sci Polym Chem Ed* 1981, 19, 2647-2650.
15. Porter, N. A.; Allen, T. R.; Breyer, R. A. *J Am Chem Soc* 1992, 114, 7676-7683.
16. Liu, W.; Nakano, T.; Okamoto, Y. *Polym J* 2000, 32, 771-777.
17. Isobe, Y.; Fujioka, D.; Habaue, S.; Okamoto, Y. *J Am Chem Soc* 2001, 123, 7180-7181.
18. Kitayama, T.; Shibuya, W.; Katsukawa, K. *Polym J* 2002, 34, 405-409.
19. Ito, M.; Ishizone, T. *Des Monomers Polym* 2004, 7, 11-24.
20. Hirano, T.; Miki, H.; Seno, M.; Sato, T. *J. Polym. Sci.: Part A: Polym. Chem.* in press.
21. Macomber, R. S. *J Chem Educ* 1992, 69, 375-378.
22. Gil, V. M. S.; Oliveira, N. C. *J Chem Educ* 1990, 67, 473-478.



23. Yuki, H.; Hatada, K.; Niinomi, Y.; Kikuchi, Y. *Polym J* 1970, 1, 36-45.
24. Nakano, T.; Matsuda, A.; Okamoto, Y. *Polym J* 1996, 28, 556–558.
25. Tanaka, T.; Habaue, S.; Okamoto, Y. *Polym J* 1995, 27, 1202-1207.

## Captions for Figures and Schemes

**Figure 1.** The relationship between polymerization temperature and  $r$  diad content of poly(NIPAAm) prepared in toluene at low temperatures in the presence of an equimolar amount of phosphate.

**Figure 2.** The relationship between polymerization temperature and  $r$  diad content of poly(NIPAAm) prepared in toluene at low temperatures in the presence of a twofold amount of phosphate.

**Figure 3.** The relationship between polymerization temperature and  $r$  diad content of poly(NIPAAm) prepared in toluene at low temperatures in the presence of a fourfold amount of phosphate.

**Figure 4.** Expanded  $^1\text{H}$  NMR spectra due to methylene and methine groups in main chain of poly(NIPAAm)s prepared (a) without phosphates at  $0^\circ\text{C}$  (Table 1, run 1), (b) with TEP at  $-40^\circ\text{C}$  (Table 3, run 8), and (c) with TBP at  $-80^\circ\text{C}$  (Table 3, run 20), respectively. \*: hexane, x: impurity.

**Figure 5.** Changes in the chemical shift of the amide proton of NIPAAm in the presence of TMP, TEP, TPP, and TBP, respectively.

**Figure 6.** van't Hoff's plots for the complexation of NIPAAm with TMP, TEP, TPP, and TBP, respectively.

**Figure 7.** Temperature dependence of the evaluated degree of association ( $\alpha$ ) of NIPAAm with TMP, TEP, TPP, and TBP, respectively.

**Figure 8.** Changes in the methylene carbon chemical shifts of NIPAAm in the presence of TBP (■) (  $[\text{NIPAAm}]_0 + [\text{TBP}]_0 = 0.25 \text{ mol/L}$  ) and of NIPAAm alone at the corresponding concentration (●), measured in toluene- $d_8$  at  $0^\circ\text{C}$ .

**Figure 9.** Job's plots for the association of NIPAAm with TBP at  $0^\circ\text{C}$  evaluated from the changes in the chemical shift of methylene carbon of NIPAAm.

**Figure 10.** Changes in the carbonyl carbon chemical shifts of NIPAAm in the presence of TBP (■) (  $[\text{NIPAAm}]_0 + [\text{TBP}]_0 = 0.25 \text{ mol/L}$  ) and of NIPAAm alone at the corresponding concentration (●), measured in toluene- $d_8$  at  $-80^\circ\text{C}$ .

**Figure 11.** Job's plots for the association of NIPAAm with TBP at  $-80^\circ\text{C}$  evaluated from the changes in the chemical shift of carbonyl carbon of NIPAAm.

**Scheme 1.** Formation of 1:1 NIPAAm-HMPA complex and propagating radical derived therefrom.

**Scheme 2.** Possible mechanism for non-stereospecific radical polymerization of NIPAAm.

**Scheme 3.** Proposed mechanism for syndiotactic-specific radical polymerization of NIPAAm complexed with an equimolar amount of Lewis base.

**Scheme 4.** Proposed mechanism for isotactic-specific radical polymerization of NIPAAm complexed with a twofold amount of Lewis base.

**Table 1.** Radical Polymerization of NIPAAm in toluene at low temperatures for 24h in the absence or presence of an equimolar amount of phosphate<sup>a</sup>

Run	Added phosphate	Temperature °C	Yield %	Diad tacticity/% <sup>b</sup>		$M_n^c$ x 10 <sup>4</sup>	$M_w/M_n^c$
				<i>m</i>	<i>r</i>		
1 <sup>d</sup>	None	0	>99	46	54	2.87	3.5
2 <sup>d</sup>	None	-20	>99	46	54	2.38	3.1
3 <sup>d</sup>	None	-40	75	44	56	2.39	2.7
4 <sup>d</sup>	None	-60	41	44	56	2.47	3.0
5 <sup>d</sup>	None	-80	18	44	56	1.72	3.2
6	TMP	0	>99	42	58	1.77	2.5
7	TMP	-20	>99	40	60	1.62	2.1
8	TMP	-40	>99	40	60	2.39	2.4
9 <sup>d</sup>	TMP	-60	>99	39	61	1.46	2.1
10 <sup>d</sup>	TMP	-80	91	43	57	1.98	2.1
11	TEP	0	>99	41	59	1.08	2.3
12	TEP	-20	>99	40	60	1.41	2.0
13	TEP	-40	>99	40	60	1.63	1.8
14 <sup>d</sup>	TEP	-60	>99	41	59	2.26	2.1
15 <sup>d</sup>	TEP	-80	58	42	58	1.19	2.5
16	TPP	0	>99	42	58	1.23	2.0
17	TPP	-20	>99	41	59	1.23	2.0
18	TPP	-40	>99	42	58	1.33	2.1
19 <sup>d</sup>	TPP	-60	93	42	58	1.76	1.9
20 <sup>d</sup>	TPP	-80	76	43	57	1.16	2.3
21	TBP	0	>99	45	55	1.28	2.0
22	TBP	-20	>99	43	57	1.89	2.6
23	TBP	-40	>99	44	56	1.46	2.3
24 <sup>d</sup>	TBP	-60	90	45	55	1.83	2.0
25 <sup>d</sup>	TBP	-80	75	47	53	1.18	2.1

a. [NIPAAm]<sub>0</sub> = 0.5 mol/L, [phosphate] = 0.5 mol/L, [*n*-Bu<sub>3</sub>B] = 0.05 mol/L.

b. Determined by <sup>1</sup>H NMR signals due to methylene group.

c. Determined by SEC (polystyrene standards).

d. Monomer and/or polymer were precipitated during the polymerization reaction.

**Table 2.** Radical Polymerization of NIPAAm in toluene at low temperatures for 24h in the presence of a twofold amount of phosphate<sup>a</sup>

Run	Added phosphate	Temperature °C	Yield %	Diad tacticity/% <sup>b</sup>		$M_n^c$ x 10 <sup>4</sup>	$M_w/M_n^c$
				<i>m</i>	<i>r</i>		
1	TMP	0	>99	41	59	2.08	2.0
2	TMP	-20	>99	39	61	1.77	1.9
3	TMP	-40	>99	39	61	2.03	1.8
4	TMP	-60	>99	41	59	1.32	2.0
5	TMP	-80	>99	48	52	1.36	2.2
6	TEP	0	>99	40	60	1.17	2.1
7	TEP	-20	>99	38	62	1.33	2.0
8	TEP	-40	>99	38	62	1.35	2.7
9 <sup>d</sup>	TEP	-60	96	39	61	1.51	1.9
10 <sup>d</sup>	TEP	-80	93	45	55	1.27	2.5
11	TPP	0	>99	40	60	1.41	1.9
12	TPP	-20	>99	39	61	1.17	2.1
13	TPP	-40	>99	40	60	1.29	1.9
14	TPP	-60	>99	41	59	1.29	2.1
15	TPP	-80	>99	49	51	0.90	2.0
16	TBP	0	>99	43	57	1.22	2.0
17	TBP	-20	>99	41	59	1.40	2.0
18	TBP	-40	>99	41	59	1.45	1.8
19	TBP	-60	>99	42	57	1.36	2.0
20	TBP	-80	>99	52	48	0.66	2.4

a. [NIPAAm]<sub>0</sub> = 0.5 mol/L, [phosphate] = 1.0 mol/L, [*n*-Bu<sub>3</sub>B] = 0.05 mol/L.

b. Determined by <sup>1</sup>H NMR signals due to methylene group.

c. Determined by SEC (polystyrene standards).

d. Monomer and/or polymer were precipitated during the polymerization reaction.

**Table 3.** Radical Polymerization of NIPAAm in toluene at low temperatures for 24h in the presence of a fourfold amount of phosphate<sup>a</sup>

Run	Added phosphate	Temperature °C	Yield %	Diad tacticity/% <sup>b</sup>		$M_n^c$ x 10 <sup>4</sup>	$M_w/M_n^c$
				<i>m</i>	<i>r</i>		
1	TMP	0	99	40	60	1.00	2.0
2	TMP	-20	96	37	63	1.10	1.9
3	TMP	-40	>99	39	61	1.38	1.8
4 <sup>d</sup>	TMP	-60	94	41	59	1.23	2.0
5 <sup>d</sup>	TMP	-80	>99	51	49	0.84	2.2
6	TEP	0	96	39	61	1.17	2.1
7	TEP	-20	90	38	62	1.22	2.0
8	TEP	-40	89	35	65	1.20	2.7
9 <sup>d</sup>	TEP	-60	>99	36	64	1.35	1.9
10 <sup>d</sup>	TEP	-80	90	50	50	0.58	2.5
11	TPP	0	>99	39	61	1.11	2.0
12	TPP	-20	88	38	62	1.11	2.1
13	TPP	-40	>99	37	63	1.28	2.0
14 <sup>d</sup>	TPP	-60	81	40	60	1.30	3.8
15 <sup>d</sup>	TPP	-80	>99	55	45	0.76	1.8
16	TBP	0	>99	39	61	1.02	2.0
17	TBP	-20	>99	38	62	1.21	2.0
18	TBP	-40	>99	37	63	1.47	2.0
19 <sup>d</sup>	TBP	-60	>99	43	57	1.15	2.5
20 <sup>d</sup>	TBP	-80	>99	57	43	0.57	2.1

a. [NIPAAm]<sub>0</sub> = 0.5 mol/L, [phosphate] = 2.0 mol/L, [*n*-Bu<sub>3</sub>B] = 0.05 mol/L.

b. Determined by <sup>1</sup>H NMR signals due to methylene group.

c. Determined by SEC (polystyrene standards).

d. Monomer and/or polymer were precipitated during the polymerization reaction.

**Table 4.** Equilibrium constants ( $K$  L/mol) for the complex formation between NIPAAm and phosphates<sup>a</sup>

Phosphate	Temperature / °C						
	60	40	25	0	-20 <sup>b</sup>	-40 <sup>b</sup>	-60 <sup>b</sup>
TMP	1.14	2.07	3.05	5.96	12.7	29.5	79.8
TEP	3.62	5.40	7.79	15.3	28.8	60.5	146
TPP	2.61	4.37	6.54	12.8	26.3	59.4	156
TBP	2.53	4.27	6.17	11.8	23.7	52.0	132

a. NMR conditions;  $[\text{NIPAAm}]_0 = 5.0 \times 10^{-2}$  mol/L, toluene- $d_8$ .

b. Calculated from van't Hoff isochor.

**Table 5.** Enthalpy and entropy for the complex formation between NIPAAm and phosphates

Phosphate	$\Delta H$ J/mol	$\Delta S$ J/mol•K
TMP	$-(2.98 \pm 0.19) \times 10^2$	$-(8.7 \pm 0.6) \times 10^{-1}$
TEP	$-(2.64 \pm 0.03) \times 10^2$	$-(6.4 \pm 0.1) \times 10^{-1}$
TPP	$-(2.89 \pm 0.11) \times 10^2$	$-(7.5 \pm 0.4) \times 10^{-1}$
TBP	$-(2.78 \pm 0.12) \times 10^2$	$-(7.2 \pm 0.4) \times 10^{-1}$



Figure 1 / T. Hirano et al.

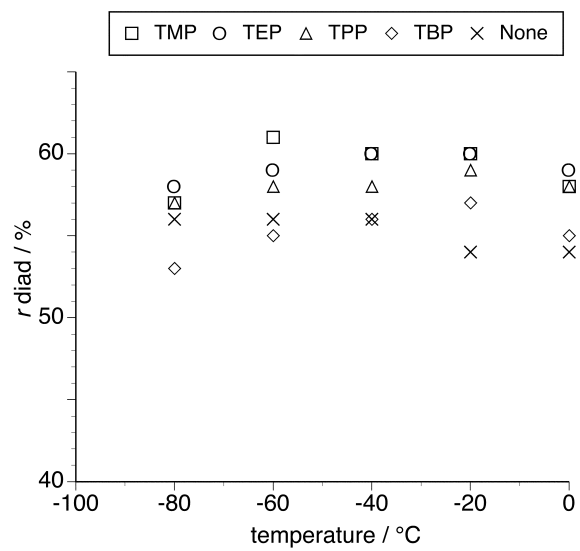


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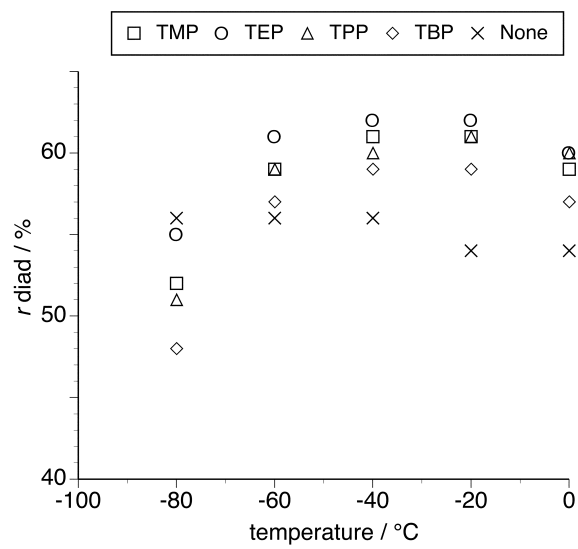


Figure 3 / T. Hirano et al.

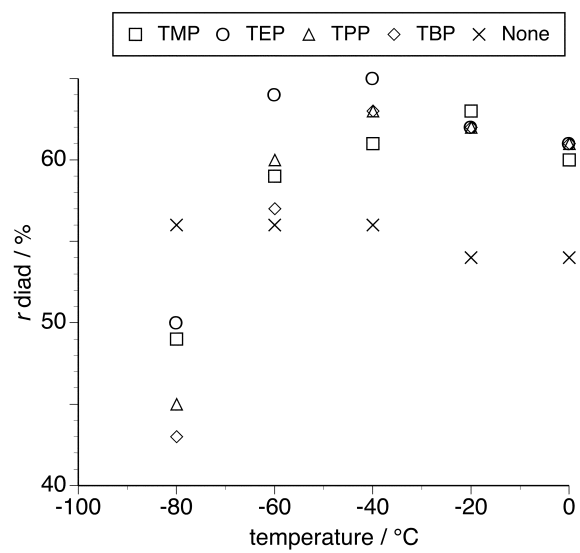




Figure 5 / T. Hirano et al.

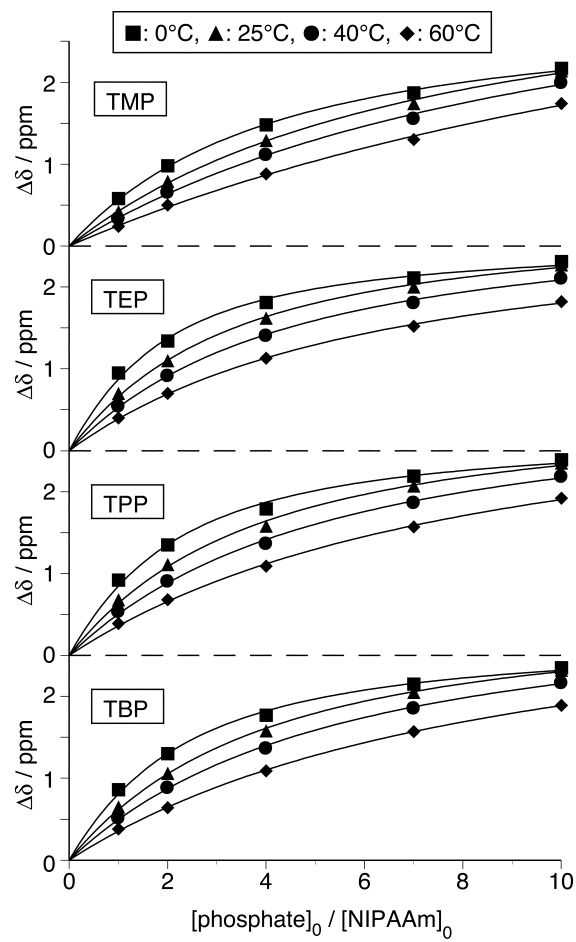


Figure 6 / T. Hirano et al.

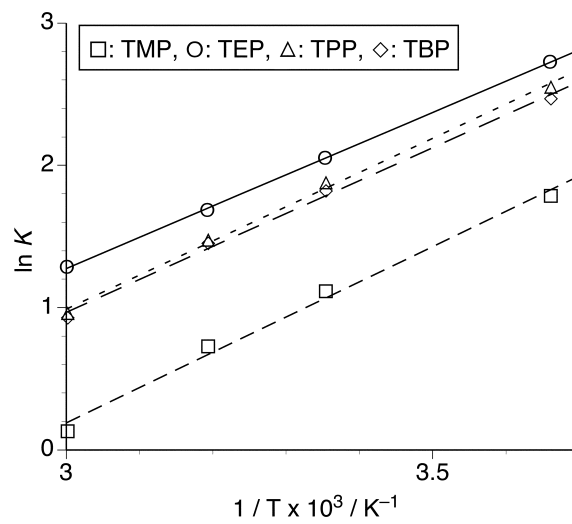


Figure 7 / T. Hirano et al.

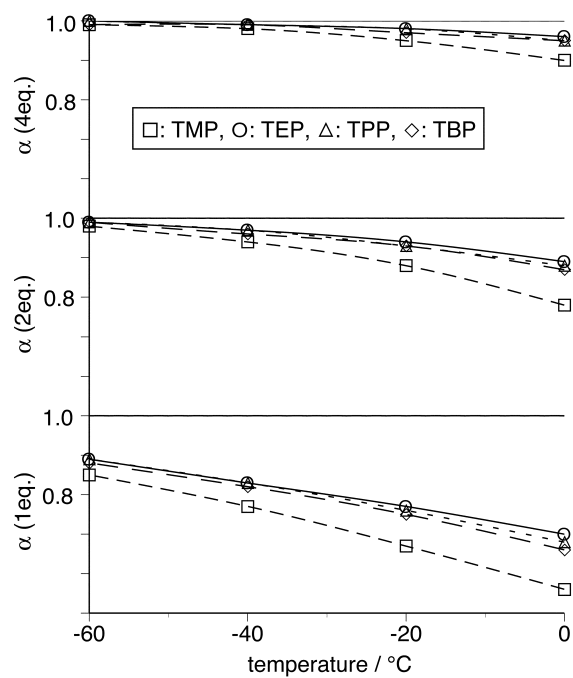


Figure 8 / T. Hirano et al.

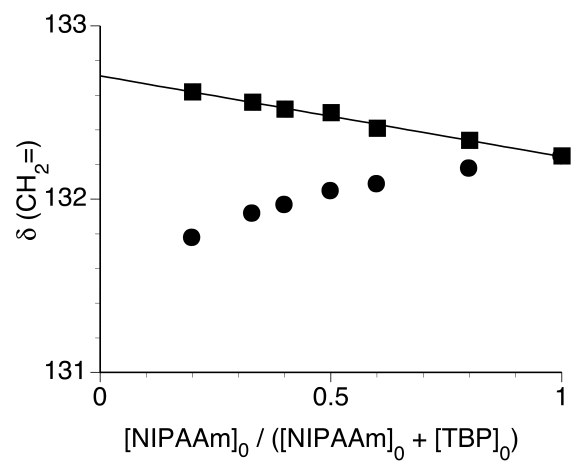




Figure 9 / T. Hirano et al.

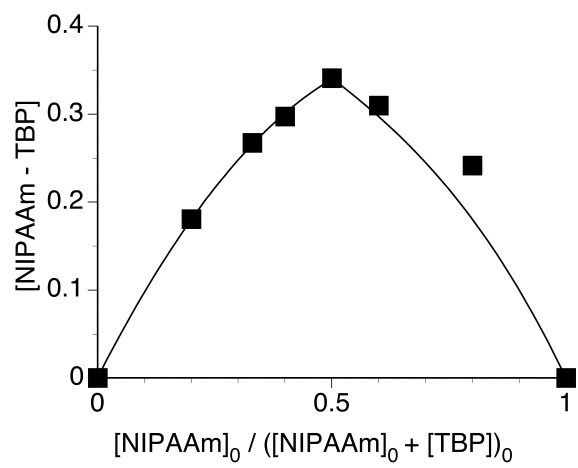


Figure 10 / T. Hirano et al.

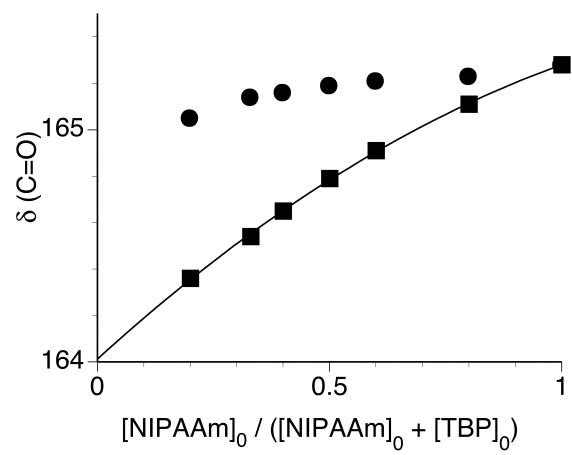
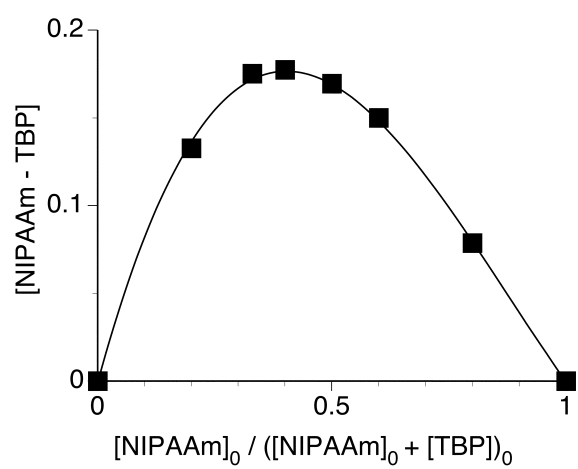
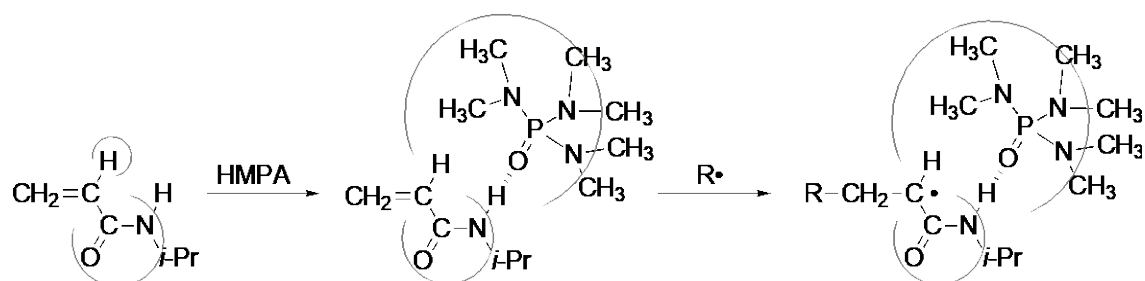


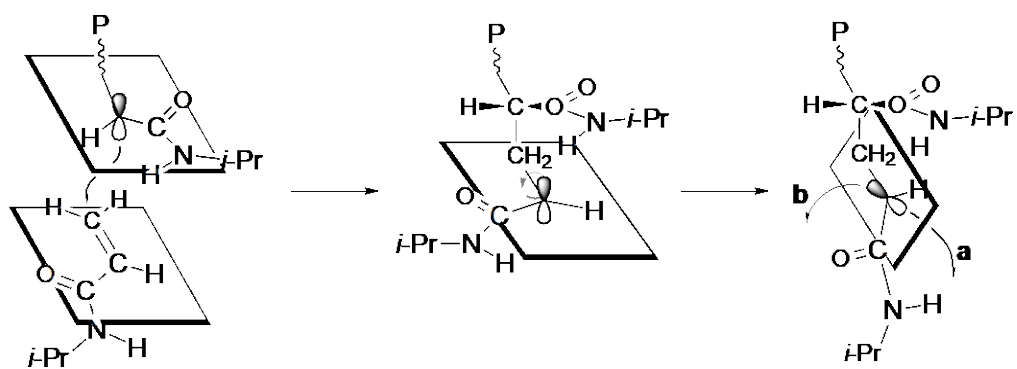
Figure 11 / T. Hirano et al.



Scheme 1 / T. Hirano et al.



Scheme 2 / T. Hirano et al.





Scheme 4 / T. Hirano et al.

